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# CERTIFICATE

This certificate is issued in support of an application for Patent registration in a country outside New Zealand pursuant to the Patents Act 1953 and the Regulations thereunder.

I hereby certify that annexed is a true copy of the Provisional Specification as filed on 21 April 1999 with an application for Letters Patent number 335321 made by AUCKLAND UNISERVICES LTD.

Dated 4 May 2000.

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Neville Harris
Commissioner of Patents

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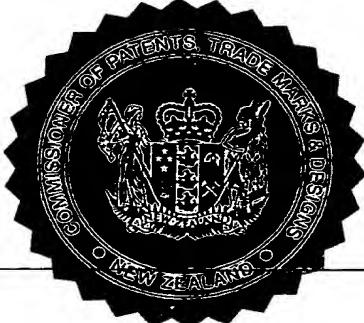
335321

Patents Form No. 4

PATENTS ACT 1953

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**PROVISIONAL SPECIFICATION**

**METHOD AND SYSTEM FOR INTERACTIVE MODELLING AND DETERMINATION OF CARDIAC FUNCTIONS**

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We, **AUCKLAND UNISERVICES LIMITED, a New Zealand company, of 58 Symonds Street, Auckland, New Zealand,** do hereby declare this invention to be described in the following statement:

# METHOD AND SYSTEM FOR INTERACTIVE MODELLING AND DETERMINATION OF CARDIAC FUNCTIONS

## FIELD OF THE INVENTION

The invention relates to a method and system for interactive modelling and determination of cardiac functions. The method and system of the invention is particularly suited to measuring cardiac function and/or mass of a ventricle of the heart of a subject. The method and system of the invention may also be used to used to calculate the volume and/or mass of other organs such as a lung or kidney, or may be used to measure the position of the wall of a blood vessel for the purposes of analysis of flow.

## BACKGROUND TO INVENTION

Ventricular mass, volumes and wall thickness at end diastole and end systole are essential clinical parameters for diagnosis and management of many cardiac diseases. Magnetic resonance imaging (MRI) is able to provide accurate and precise estimations of ventricular mass, volume and wall thickness, since it is a true 3-dimensional method which is not dependent on geometric assumptions and is not limited in the position or orientation of the possible images, unlike other methods, for example, echocardiography or computed tomography.

Recent advances in MRI allow the acquisition of 10 to 20 MRI images or slices in short and long axis or arbitrary orientations, each with 10 to 25 frames through the cardiac cycle in approximately 15 minutes, which is a clinically acceptable time. Previous studies have shown that the summation of areas outlined in short axis MRI slices gives more accurate and reproducible estimates of volume than echocardiography or LV angiography.

A major limitation of the MRI slice summation method is the prohibitive time required to outline the endocardial and epicardial boundaries of the left ventricle in each slice. This severely limits application of the use of the technique to routine clinical care.

In the past, many semi-automated image segmentation algorithms have been applied to this problem, but these solutions are frequently not sufficiently robust and accurate for routine clinical use. In particular the image pixel intensities are insufficient to adequately constrain the segmentation problem, due to the limited temporal and spatial resolution, presence of image artifacts and lack of contrast between blood and muscle. The amount of time spent on manual editing and correction of contours obtained from these previous solutions renders automated methods nearly as slow as manual contouring in clinical practice.

## SUMMARY OF INVENTION

In broad terms the invention comprises a method for measuring characteristics of an organ or part thereof of a subject, from multiple image slices of subject's organ or part thereof, the method comprising the steps of defining the spatial position of at least two of the slices; determining the position of anatomical land marks of the organ or part thereof from two or more of the slices for which the spatial positions have been defined; defining a number of boundary guide points on one or more slices for which the spatial positions have been defined; converting the guide points to three-dimensional coordinates; defining a reference model of the organ or part thereof scaled and transformed according to the anatomical land marks of the subject's organ or part; forming an estimate model by fitting the reference model to the guide points; and calculating the characteristics from the estimate model. The organ or part thereof may be a heart ventricle and the left ventricle in particular, or a lung or kidney, or the wall of a blood vessel, for example. Where the organ is a ventricle of the subject's heart, the boundary guide points may be a number of endocardial and/or epicardial boundary guide points.

Preferably the method further comprises the steps of calculating the volume of the subject organ or part from multiple image slices, obtained from multiple frames taken at various time intervals; defining the temporal position of at least two of the slices; defining a number of boundary guide points on one or more slices for which the temporal positions have been defined; converting the guide points to four-dimensional coordinates and fitting the estimate model to each temporal position.

Preferably the position of the anatomical land marks of the organ or part are defined in three-dimensional spatial coordinates.

Preferably one or more of the anatomical land marks allows the length and position of the long axis of the organ or part thereof to be determined.

Preferably the method further comprises the step of calculating the mass of the subject organ or part.

Preferably the organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle or part thereof.

Preferably the organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through changes in wall thickness over time.

Preferably the organ comprises a kidney and the characteristics measured include cortical thickness.

**BRIEF DESCRIPTION OF DRAWINGS**

A preferred form of the invention will now be described, by way of example, with reference to the accompanying drawings in which:

Figure 1 is a flow chart outlining the method of the invention;

Figure 2 shows the main window of the application program in which the invention is implemented;

Figure 3 shows a guide points window and the preferred method of selecting the left ventricular basal slice from this window;

Figure 4 shows the preferred method of selecting the left ventricular apical slice from the window of Figure 3;

Figure 5 shows the preferred method of defining the base or mitral valve plane from the window of Figure 3;

Figure 6 shows the preferred method of entering characteristics of the right ventricle from the window of Figure 3;

Figures 7 to 10 illustrate a method of selecting boundary guide points from the window of Figure 3; and

Figures 11 and 12 show a preferred window for viewing the model.

## DETAILED DESCRIPTION OF PREFERRED FORMS

A number of images are first obtained of the left ventricle of a subject. The images may be acquired from an MRI scanner. Images may alternatively be obtained by an ultra-fast CT or 3-dimensional ultrasound machine. The images are typically 2-dimensional cines or movies of the heart and are taken at standard orientations, for example, short axis and long axis, or at entirely arbitrary positions depending on the nature of the pathology and imaging modality.

The preferred images are acquired in a number of spatial locations, having a lowest or apical slice, a highest or basal slice, one or more middle slices and one or more long axis slices. The preferred images are acquired in between 10 and 20 spatial locations, and typically 12 spatial locations. Preferably images in each of these spatial locations are obtained at multiple frames through the cardiac cycle. The preferred number of frames is 10 to 25.

Conventional MRI imaging apparatus produces images having image headers. The image header in each image generally comprises an extensive data list including patient name and scan parameters at the beginning of each image. The image header also provides data representing the spatial position and temporal position of each slice or frame.

Figure 1 sets out the basic method of the invention. The step of obtaining the images is indicated at 10. The next step indicated at 12 is to load the images into a memory. The preferred memory forms part of a computer having a CPU, input devices and a

display device such as a VDU. The preferred input devices comprise a keyboard, mouse and disk drive, typically a networked magneto-optical disc drive and/or CD ROM drive. Images may also be transferred over a network. The preferred memory comprises a hard disk drive suitable for storing the images.

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The preferred computer comprises a SUN SparcStation, SGI work station, or similar having approximately 128 MB Ram or similar. The computer has loaded on it suitable operating system software, such as SOLARIS or IRIX. The preferred computer is arranged to execute application software in which the present invention has been developed. The preferred application software is written in C++, using OpenGL, OpenInventor and Xwindows for graphical interfaces.

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Referring to Figure 2, the user is presented with a main window from which a number of options may be selected. The option to load planes is indicated at 14 which loads the three-dimensional position of the images and the option to load frames is indicated at 15 which loads the position of the images in time. This spatial and temporal information is generally included in the image headers. The option to load images is indicated at 16. Each separate image location is displayed in a second window at the first phase of imaging simultaneously.

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Various parameters may be specified by the user at the time of loading the images, for example Model Type, Fit Type and Data Set. The user may also specify directory names for directories such as a Data Directory, a Model Directory and a Script Directory.

25

As shown at step 18 in Figure 1, the next step is to define the length and position of the long axis of the left ventricle from two of the slices for which the spatial positions have been defined. The main window of Figure 2 presents to the user an option to enter the guide points editor.

30

The guide points editor loads the editor window shown in Figure 3. The editor window includes panel 20 which displays thumbnail images of the images stored in the memory. Panel 22 displays an enlarged image of one of the images displayed in panel 20. The preferred form window shown in Figure 3 also provides the user with the ability to zoom and pan images and to adjust brightness and contrast. The user may

35

select the image to be displayed in panel 22 by, for example, clicking or preferably double clicking on one of the thumbnails displayed in panel 20.

5   The user first selects the basal or highest short axis slice in panel 20, double clicking on the thumbnail image to display the enlarged image in panel 22. In Figure 3 the user has selected the basal slice which is described below panel 22 as the seventh short axis image obtained during the first time interval or frame.

10  The user selects the Base option indicated at 24. A prompt is displayed for the user to pick a point to represent the base in the model's cardiac coordinate system. The user selects a point in the centre of the ventricular image by clicking in panel 22. This point will represent the highest point of the object. Once the desired base has been selected the user selects the option to accept the base indicated at 26.

15  Referring to Figure 4, the user repeats the procedure to select the apex of the object. The user selects the Apex option indicated at 28. A prompt is displayed for the user to pick a point representing the apex and the user then selects the point in panel 22. Once the desired apex has been selected the user accepts the apex as indicated at 30.

20  If the spatial position of the basal slice and the apical slice is known then anatomical land marks may be determined, for example the long axis. The software calculates the length and position of the long axis by defining a line in 3-dimensional space between the two points selected by the user.

25  As shown in Figure 5, the user may display in panel 22 an image taken of the long axis of the object, as indicated by the description below panel 22. The user selects the Base Points option 32 which then prompts the user to choose two or more points on the image to define the mitral valve plane.

30  The user selects the points by clicking in panel 22 and once the desired points have been selected the user accepts the base points indicated at 34. Further options may also be provided, for example advancing the image displayed in panel 22 to the next frame.

35  It will be appreciated that the user does not need to define the axis by selecting the centre of the ventricle in the basal and apical slices. The user may instead define the

centre of the left ventricle in two slices which are not the basal or apical slices. The software may then calculate the position of the long axis by defining a line in 3-dimensional space between these two points. The length of the long axis of the left ventricle may then be calculated separately from the distance between the basal and apical slices if the spatial position of the slices is known.

As shown in Figure 6, the user is not limited to measuring characteristics of the left ventricle. By selecting the option indicated at 35 the user may measure characteristics of the right ventricle of the subject.

As shown at 36 in Figure 1, the next step is to define a number of guide points on one or more slices for which the spatial positions have been defined. Referring to Figure 7 the user is presented with the option indicated at 38 of defining guide points. The user then selects and displays in panel 22 any one of the slices stored in the memory.

The user first selects the active surface which is being defined as indicated at 40. In Figure 8 the user has selected the left ventricular endocardial boundary as the active surface. Using a mouse, the user defines a number of boundary guide points on the selected slice by clicking in panel 22. These guide points define the endocardial or epicardial boundaries of the heart. Preferably three to four endocardial boundary guide points and three to four epicardial boundary guide points are entered for each slice, although the user is able to enter a large number of boundary guide points for a particular slice or may instead ignore a slice and enter no boundary guide points for it.

Once the user has defined the appropriate number of guide points, the user selects the Update Model option indicated at 42 to convert these guide points to three-dimensional coordinates from the image position in space for each boundary guide point, and fit the model.

Where a number of image frames are stored in memory, the user may advance to the next frame by clicking on the Next Frame option indicated at 43.

Figures 9 and 10 further illustrate the process by which the boundary points are defined by the user. The user is defining the endocardial boundary of an image slice different to the one shown in Figure 7. In Figures 9 and 10 the user is defining the epicardial and endocardial boundaries respectively for a further image.

As shown at step 44 in Figure 1, the software defines a reference model of a left ventricle. The preferred reference shape closely approximates the generic shape of a left ventricle. The reference model may be constructed from real patient data, but does not have to be absolutely accurate in terms of an individual patient. The reference model may be defined as an analytical function, as a coordinate system, or as data points.

The preferred reference model is a finite element model consisting of at least 16 elements, typically 16 to 40, each with cubic interpolation in the circumferential and longitudinal directions. Linear interpolation is used to couple the endocardial and epicardial surfaces into a coherent 3-D model. The preferred model is defined in a polar coordinate system in which the radial coordinate of the model is fitted as a function of the two angular coordinates in the circumferential and longitudinal directions respectively. The preferred initial shape of the reference model is a regular ellipsoid, typically a prolate spheroid, obtained by setting the endocardial and epicardial surfaces to a constant radial value. The preferred reference model is scaled according to the length of the long axis of the left ventricle of the subject with the extent of the model in the longitudinal direction set to correspond to the point identified on the most basal slice of the left ventricle in the long axis.

The preferred estimate model is obtained by a least squares finite element modelling process in which the left ventricle is divided into a number of rectangular segments or elements. Each element defines a bicubic spline surface for part of the endocardial and epicardial surfaces of the left ventricle. It is important to ensure continuity in the surface defined by adjacent elements. To ensure continuity, adjacent elements are constrained to have the same position and slope on each side of the join. Ensuring continuity in this way eliminates or at least reduces ridges and sharp transitions between adjacent elements.

The model is prescribed in a prolate spheroidal coordinate system $(\lambda, \mu, \theta)$ where

$$x = f \cosh(\lambda) \cos(\mu)$$
$$y = f \cosh(\lambda) \sin(\mu) \cos(\theta) \qquad (2)$$
$$z = f \sinh(\lambda) \sin(\mu) \sin(\theta)$$

Previously defined points are used to determine the initial position of the model with respect to the images. These are:

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a)  the location of the central axis at the center of the LV in an apical short axis image

b)  the location of the central axis at the center of the LV in a basal short axis image

c)  the approximate centroid of the right ventricle

d)  a set of points describing the mitral valve plane.

10  A model-based coordinate system is then constructed with the origin placed on the central axis of the LV one third of the distance from the base to the apex. Nodes are placed at equally spaced intervals in the two angular coordinates ($\mu$, $\theta$) and at a constant radial coordinate ($\lambda$). The centroid of the RV has $\theta=0$ and the extent of the model in the $\mu$ direction is governed by the basal margin points. The distance from

15  apex to base is used to determine the focal length of the prolate system and provides an overall scale factor for the LV.

Within each element, the geometric coordinate field $x$ is given as a function of element or material coordinates $\xi$ by a weighted average of nodal values:

20

$$x(\xi_1, \xi_2, \xi_3) = \sum_n \Psi_n(\xi_1, \xi_2, \xi_3) x^n \qquad (1)$$

where $x^n$ are the nodal values and $\Psi_n$ are the element basis functions.

25

Each guide point is projected onto the model along lines of constant $\mu$ and $\theta$ and only the $\lambda$ field is fitted by linear least squares.

It will be appreciated that where an organ other than the left ventricle is to be

30  modelled, the reference model will be varied. For example, where the invention is used to model the right ventricle, lung and/or kidney, a different reference model will be defined.

The next step indicated at 46 in Figure 1 is to form an estimate model by fitting the

35  reference model to the guide points. Preferably this process is initiated automatically

whenever the user selects the Update Model option indicated at 42 in Figures 7 to 10. Alternatively or additionally the process may be initiated automatically whenever the user selects the Next Frame option indicated at 43 in Figures 7 to 10, or may be updated automatically in real time with any change in guide point position.

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The preferred method for incorporating the reference model data is to minimise an error function consisting of the sum of a smoothing term and a term penalising the distance between each boundary guide point and the corresponding reference model position.

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The preferred smoothing term penalises changes in slope and curvature around the left ventricle, allowing the reference model to realistically interpolate guide point data where the data is sparse.

15 The preferred penalty is introduced into the least squares method which penalises only the sum of the squared deviations from the boundary guide points to the reference model surface. In particular, the first and second derivatives of the surfaces are constrained to be minimised within the least squares fit to prevent rippling and other abnormalities. In this sense, the smoothing can be viewed as weighting the estimate 20 model more toward the reference model than the boundary guide points so that the reference model is imposed more strongly where there are no or insufficient boundary guide points.

One preferred smoothing method is set out more particularly below, in which 25 the error function minimised is:

$$E = S(\lambda) + \sum_{g} \left( \lambda(\xi_g) - \lambda_g \right)^2 \qquad (3)$$

where $S(\lambda)$ denotes the smoothing term, $\lambda_g$ are the $\lambda$ values for the guide points and 30 $\lambda(\xi_g)$ denotes the $\lambda$ values of the corresponding model points.

$S(\lambda)$ is a weighted Sobolev norm which penalizes the displacement of the estimate model from the reference model.

$$S(\lambda) = \int_{\Omega} \alpha_1 \left[ \frac{\partial u}{\partial \xi_1} \right]^2 + \alpha_2 \left[ \frac{\partial u}{\partial \xi_2} \right]^2 + \beta_1 \left[ \frac{\partial^2 u}{\partial \xi_1^2} \right]^2 + \beta_2 \left[ \frac{\partial^2 u}{\partial \xi_2^2} \right]^2$$

$$+ \gamma_1 \left[ \frac{\partial^2 u}{\partial \xi_1 \partial \xi_2} \right]^2 + \gamma_2 \left[ \frac{\partial^2 u}{\partial \xi_1 \partial \xi_3} \right]^2 + \gamma_3 \left[ \frac{\partial^2 u}{\partial \xi_2 \partial \xi_3} \right]^2 d\Omega \tag{4}$$

where $u = \lambda - \lambda^*$ where $\lambda^*$ is the reference model. The weights $\alpha_1$ and $\alpha_2$ penalize the slope of the displacement field in the circumferential and longitudinal directions respectively, the weights $\beta_1$ and $\beta_2$ penalize curvature and the weights $\gamma_1$, $\gamma_2$ and $\gamma_3$ couple slopes between directions. Typical smoothing weights are $\alpha_1 = \alpha_2 = 0$, $\beta_1 = \beta_2 = 0.001$, $\gamma_1 = \gamma_2 = \gamma_3 = 0.01$.

The resulting estimate model incorporates endocardial and epicardial boundary guide points, the long axis of the left ventricle, reference model data and smoothing constraints to produce endocardial and epicardial left ventricular surfaces in three or four dimensions closely approximating the true surfaces represented in the images.

Having defined these surfaces, the software may then calculate the intersection of the image slices with the surfaces. The intersections are each represented by two lines, one line representing the endocardium and the other line representing the epicardium which are close to the edges on the images.

Having calculated endocardial and epicardial surface boundaries on each image, the software may then perform local image processing to further improve the quality of the left ventricle boundary edges displayed in the images. The use of local image processing is not essential to the invention. Where provided, it may be invoked by the user. An edge is characterized by an abrupt change in intensity indicating a boundary, and is called a discontinuity. In general an edge is often seen as a slow change in grey level values between connected pixels. While a boundary edge may be readily apparent to the human eye, it can be difficult for software to detect.

Prior art methods of detecting discontinuities or edges include running a mask or window over the image, or by applying a known edge enhancing filter such as a

Roberts, Sobel or Laplacian operator. Applying such a filter to an entire image in order to find boundary edges is computationally expensive.

5   Using the present invention, the endocardial and epicardial boundaries have been estimated with the estimate model. The software therefore can calculate the likely position of a boundary edge in an image. An *a priori* technique may then be applied to guide the search for the boundary in the image.

10   In one method, radial lines may be drawn extending through both the endocardial and epicardial boundaries. An edge filter may be applied at the intersection of these boundaries and the radial line to determine the points on the radial line most likely to represent the endocardial and epicardial edges.

15   Further local processing could also include thresholding, for example grey-scale thresholding. All pixel values falling between two threshold values $T_1$ and $T_2$ retain their grey-scale values but all pixel values outside this interval are set to zero. Such multiple thresholds may be applied to reduce the number of grey-level values in an image, thereby enhancing the contrast. Thresholding may be applied, for example, to contrast the area in the image inside the endocardial boundary, from the area between 20   the endocardial and epicardial boundaries, and/or the area outside the epicardial boundary.

Local image processing and thresholding as described above may generate additional data points which may be added to the existing boundary guide points. The estimate 25   model contour may then be redefined based on the additional data points so that the relationship to the actual images is improved.

The additional data points obtained from local image processing and thresholding may be assigned less weight than boundary guide points selected by the user, as it will be 30   appreciated that these additional data points may be less reliable than those selected by the user. The generated data points may be displayed to the user in order to identify where additional guide points are needed to improve the estimate model, for example, where a contour has missed the actual edge.

35   It will be appreciated that where image processing is performed, it is performed at a local level. The software knows that the edge is in a particular region. Image

processing is computationally expensive and in the past has been performed on an entire image or slice. Using the invention, it is possible to determine the approximate position of the region so that image processing can be concentrated on that region, significantly reducing the processing time.

5

The software may then define the final estimate model surfaces from the finite element modelling process, with the inclusion of data points obtained by local image processing. The intersection of this surface with the image slices permits the software to display on the original images the left ventricular endocardial and epicardial

10    boundary walls. The step of drawing the estimate model is indicated in Figure 1 at 52.

As shown in Figure 2, the main window presents to the user the option of viewing the images in three dimensions, indicated at 54. On selecting this option the user is presented with a 3D viewer window as will be more particularly described with

15    reference to Figures 11 and 12.

Referring to Figure 11, the window includes panel 56 in which images are displayed. The user has the option of selecting image planes as the desired view as indicated at 58. Where the Image planes option is selected, the user may select which image slices

20    to display in panel 56. In Figure 11 the user has selected the long axis slice and the fifth short axis slice to display in panel 56. Also displayed in panel 56 are the estimate boundary walls.

Referring to Figure 12, the user has elected not to display image planes. The image

25    displayed in panel 56 is instead the estimate endocardial surface rather than individual image planes.

Each boundary or contour is then assessed by the user for appropriateness. If the boundary or contour is unacceptable, the user may define further boundary guide

30    points until such time as the boundary or contour is acceptable, as indicated in Figure 1 at 58.

Left ventricular cardiac volume, for example, may then be estimated by calculating the volume bounded by the estimate model in the step indicated at 60 in Figure 1. Left

35    ventricular wall thickness may also be calculated from the estimate model. Left ventricular mass may be calculated from the difference between the volumes enclosed

by the endocardial and epicardial contours multiplied by an appropriate constant, for example 1.05 g/ml.

It will be appreciated that the volume, wall thickness and mass of the right ventricle 5 may also be calculated in the same way. Where more than one frame is stored in the memory, the method may be used to measure abnormalities in the left or right ventricle identified through changes in wall thickness over time.

The method may also be used to measure characteristics of other organs for example 10 the lung, the kidney or may be used to measure the wall of a blood vessel. In the case of a kidney the method may be used to measure cortical thickness.

The foregoing describes the invention including preferred forms thereof. Alterations and modifications as will be obvious to those skilled in the art are intended to be 15 incorporated within the scope hereof.

RUSSELL McVEAGH WEST WALKER

per
ATTORNEYS FOR THE APPLICANT

**10** OBTAIN IMAGES

**12** LOAD IMAGES INTO MEMORY

**18** DEFINE LONG AXIS, MITRAL VALVE PLANE

**36** DEFINE GUIDE POINTS

**44** DEFINE REFERENCE MODEL

**46** DEFINE ESTIMATE MODEL CONTOUR

**52** DRAW ESTIMATE MODEL

**58** ACCEPT?

No

Yes

**60** CALCULATE VOLUME AND MASS
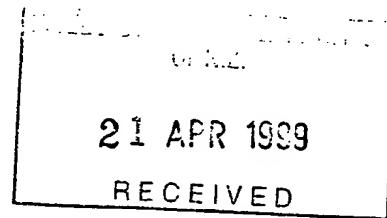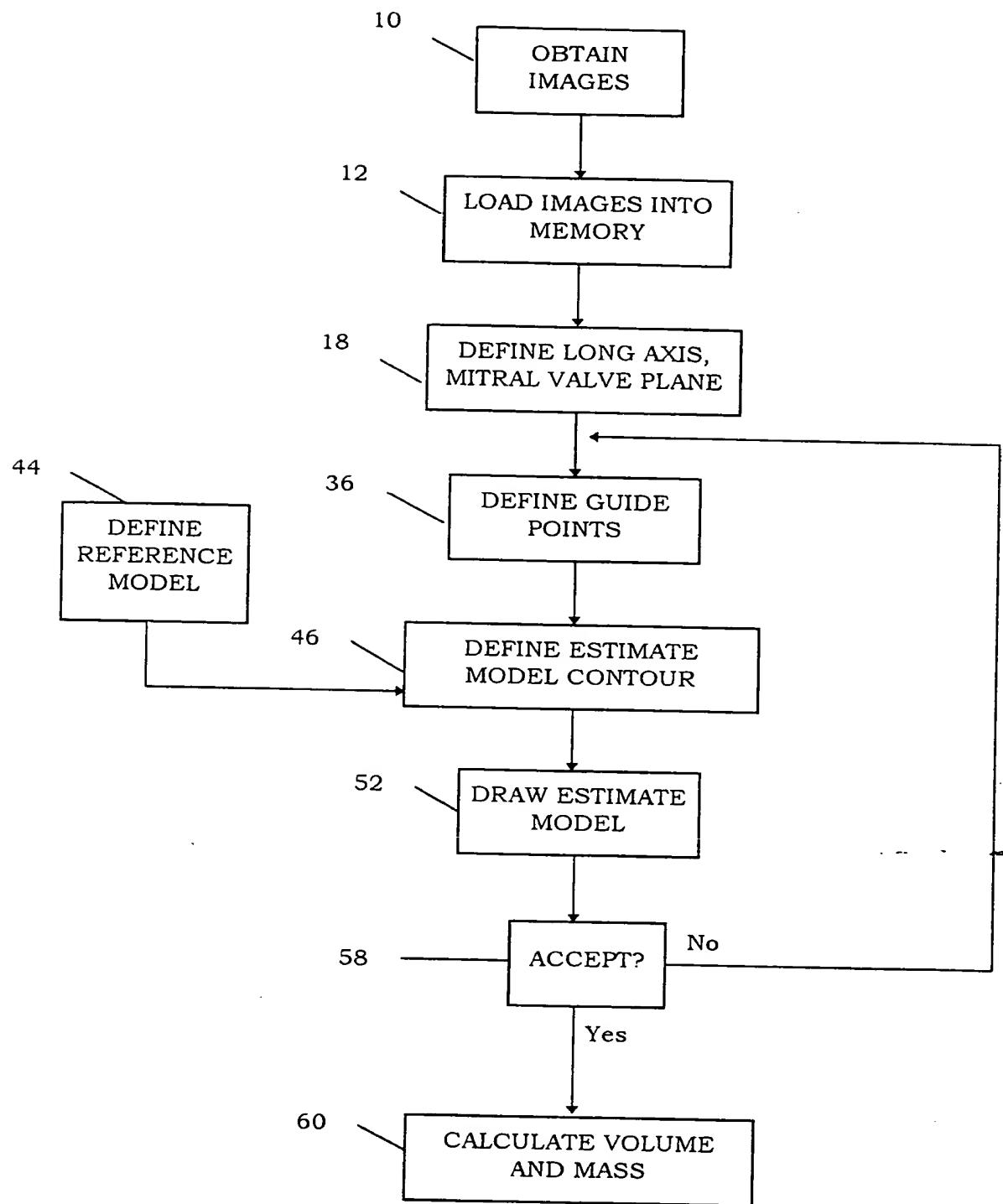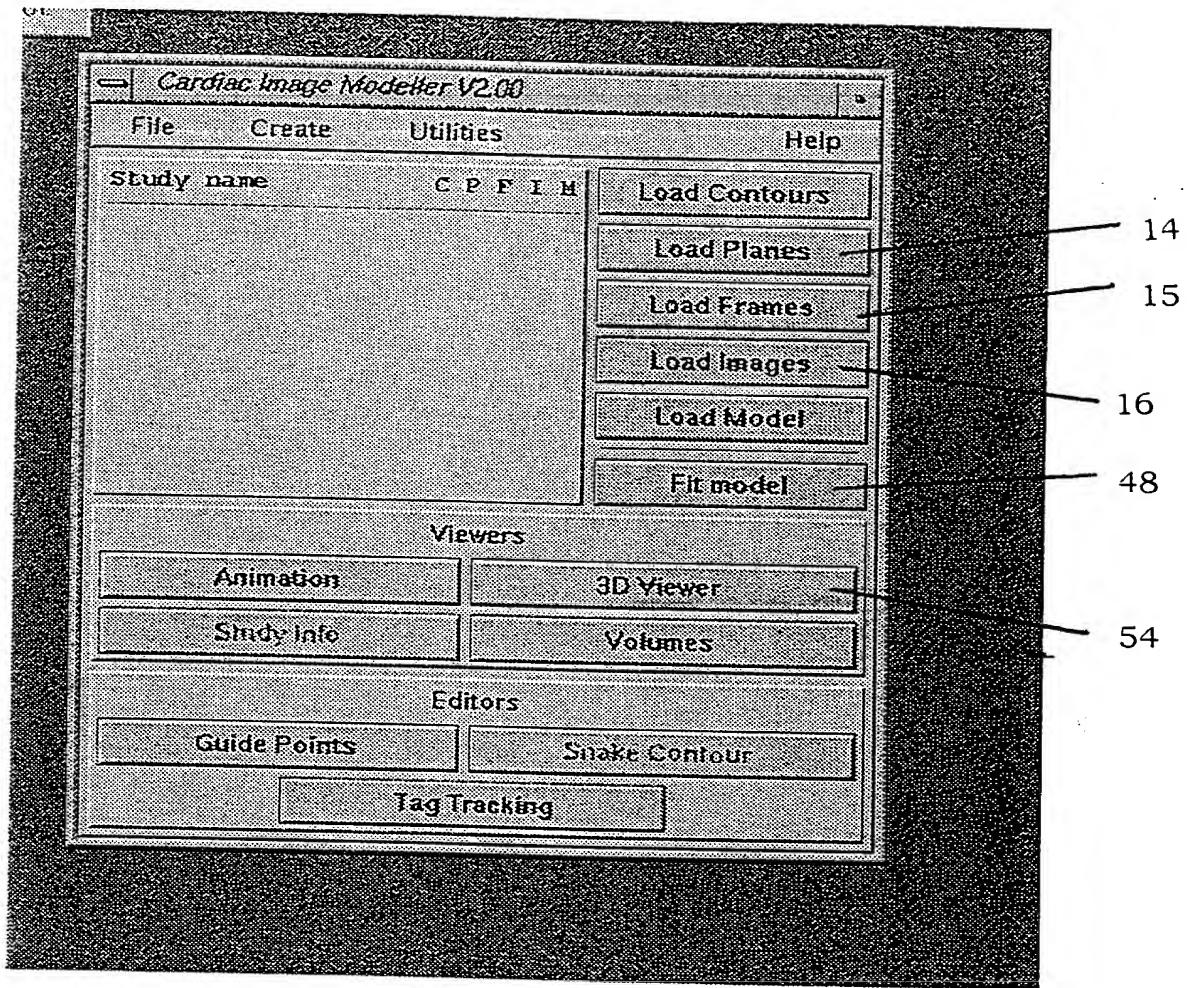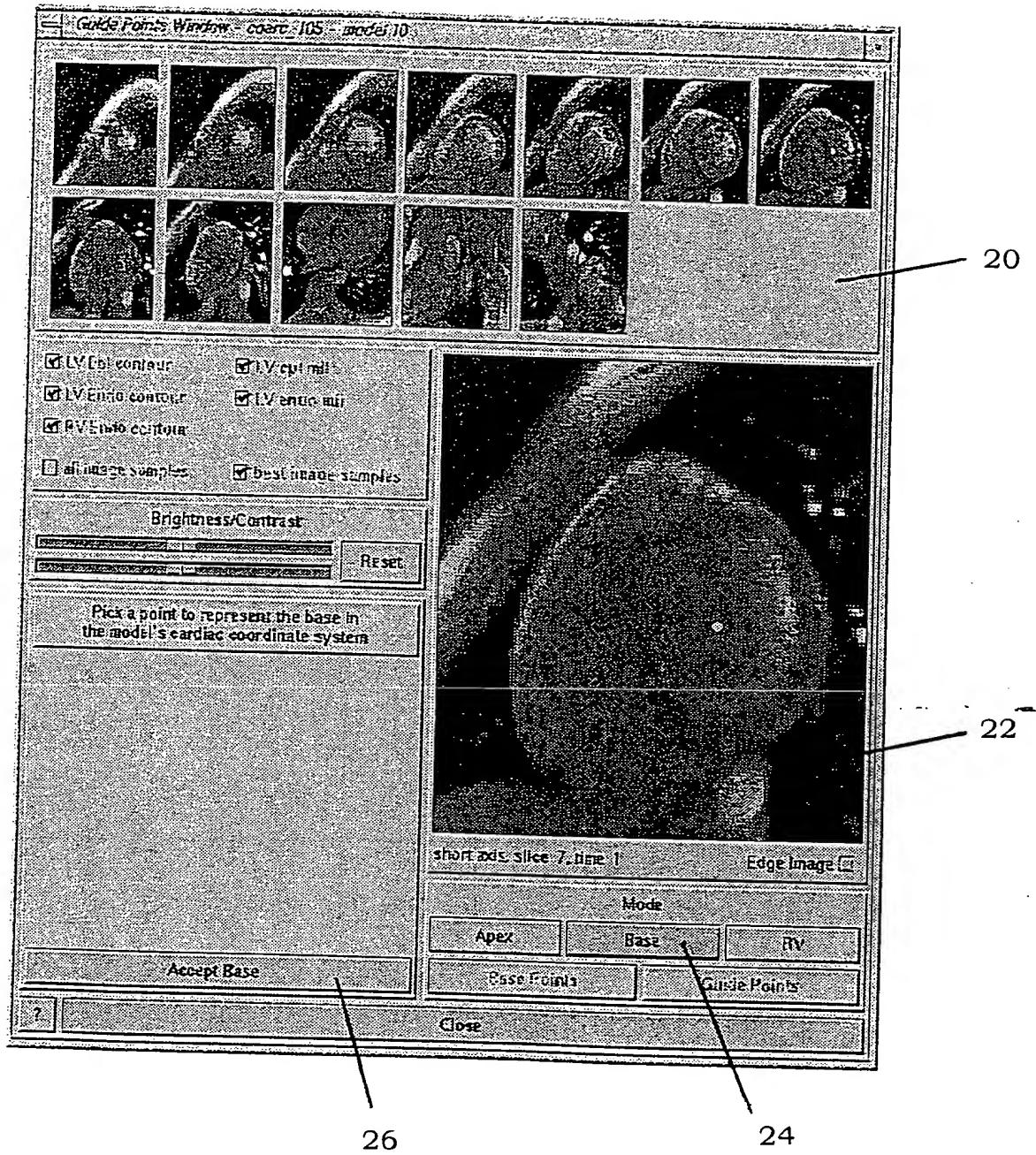
**FIGURE 1**

FIGURE 2

FIGURE 3
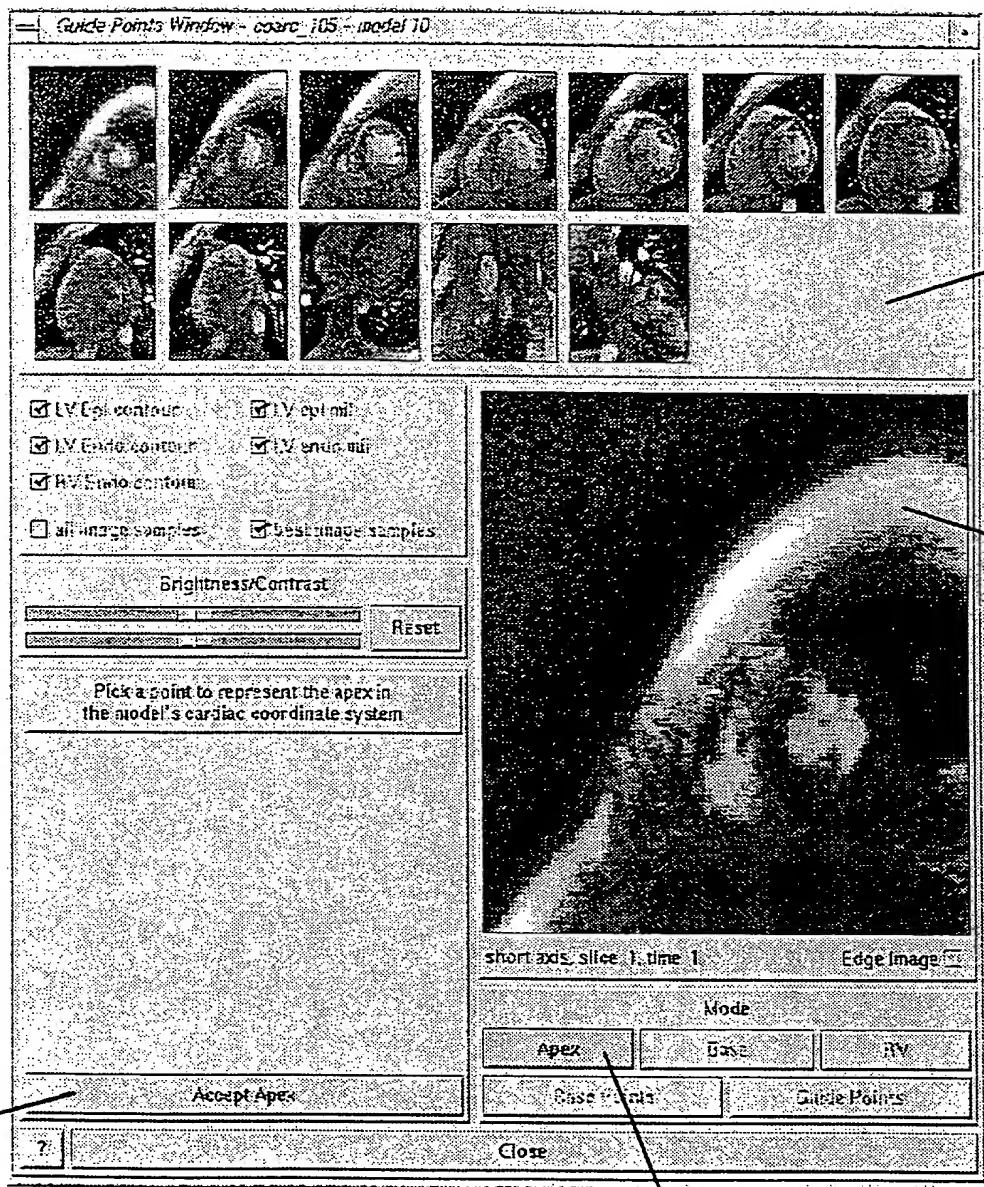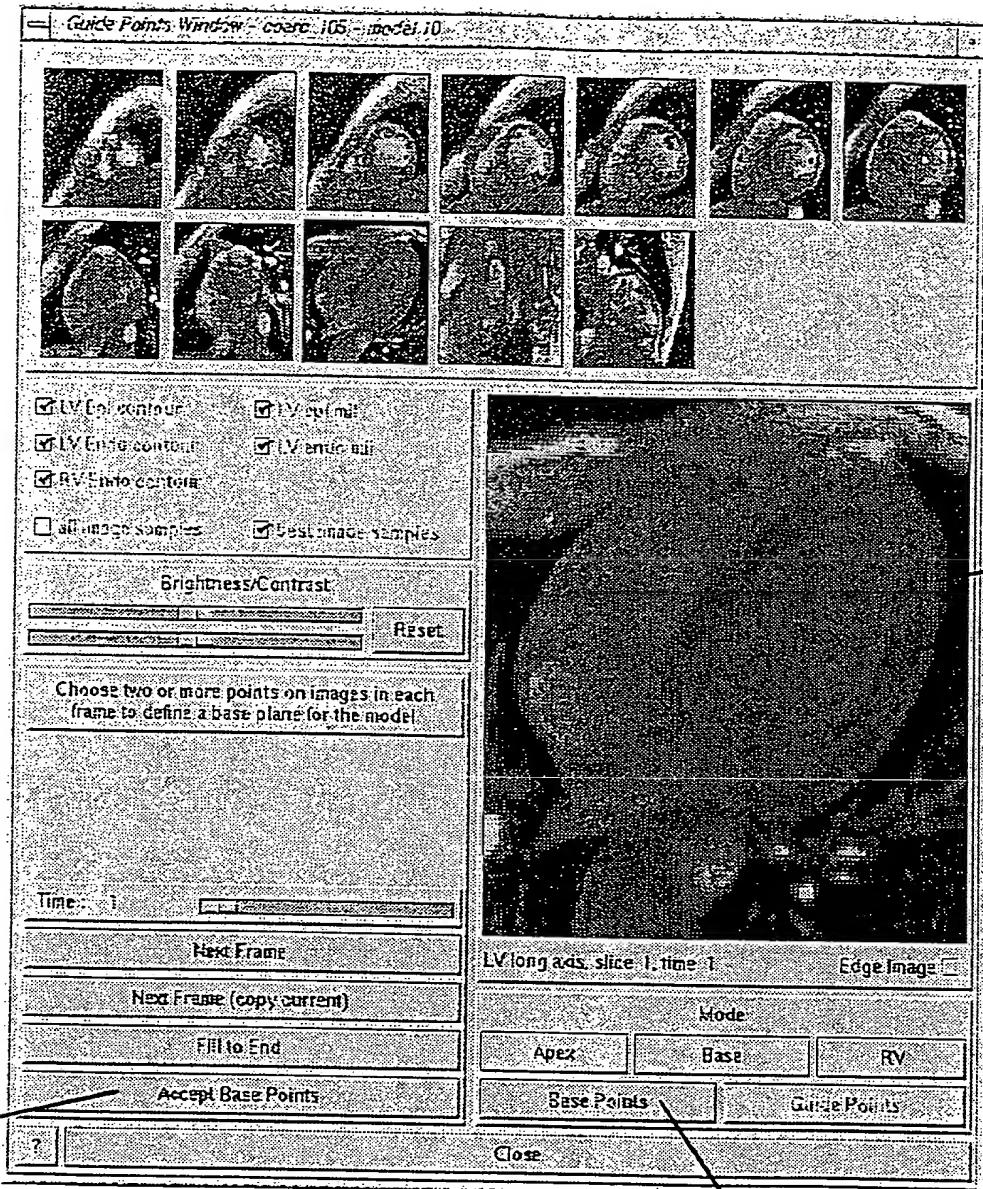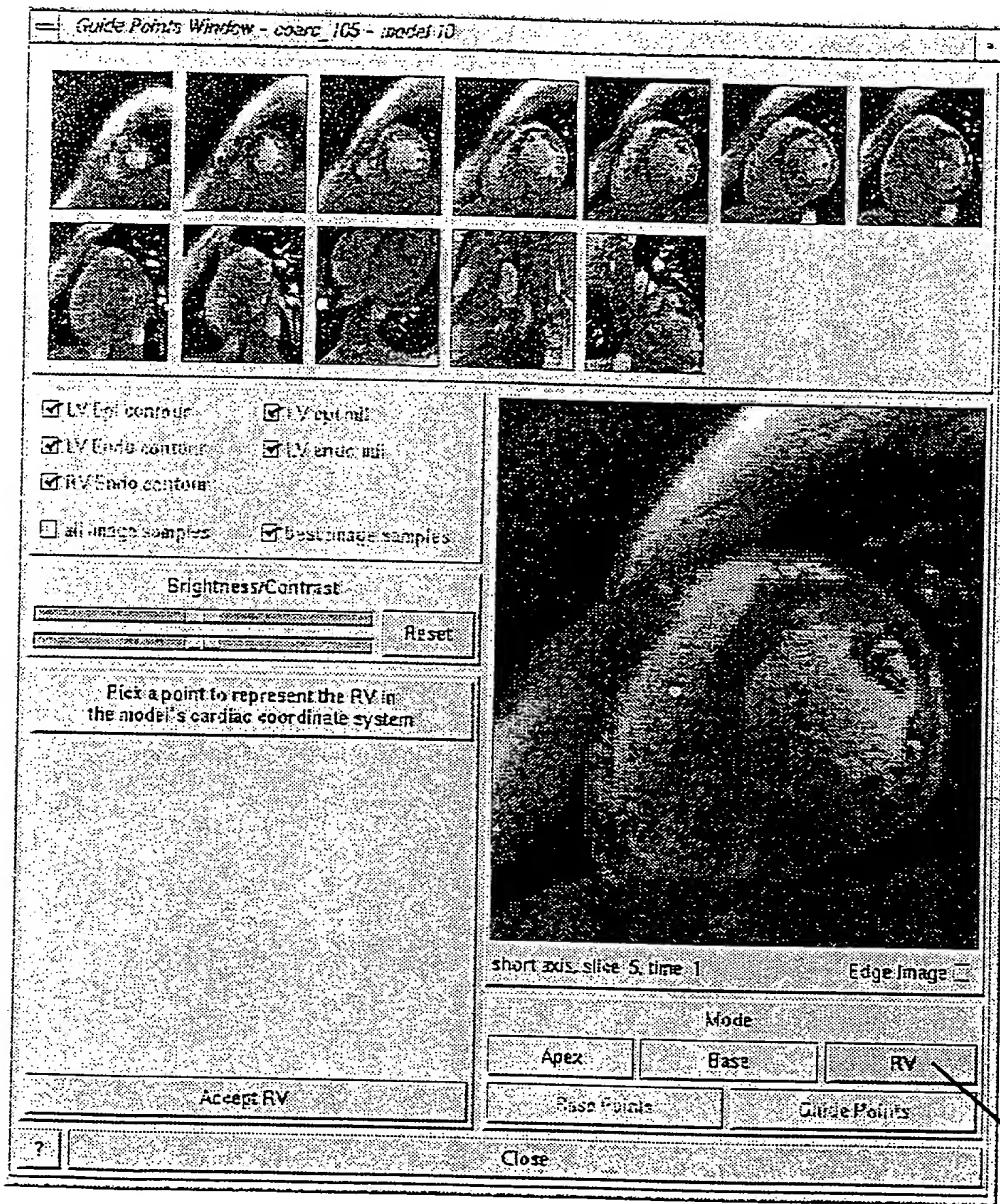
FIGURE 4

FIGURE 5

FIGURE 6
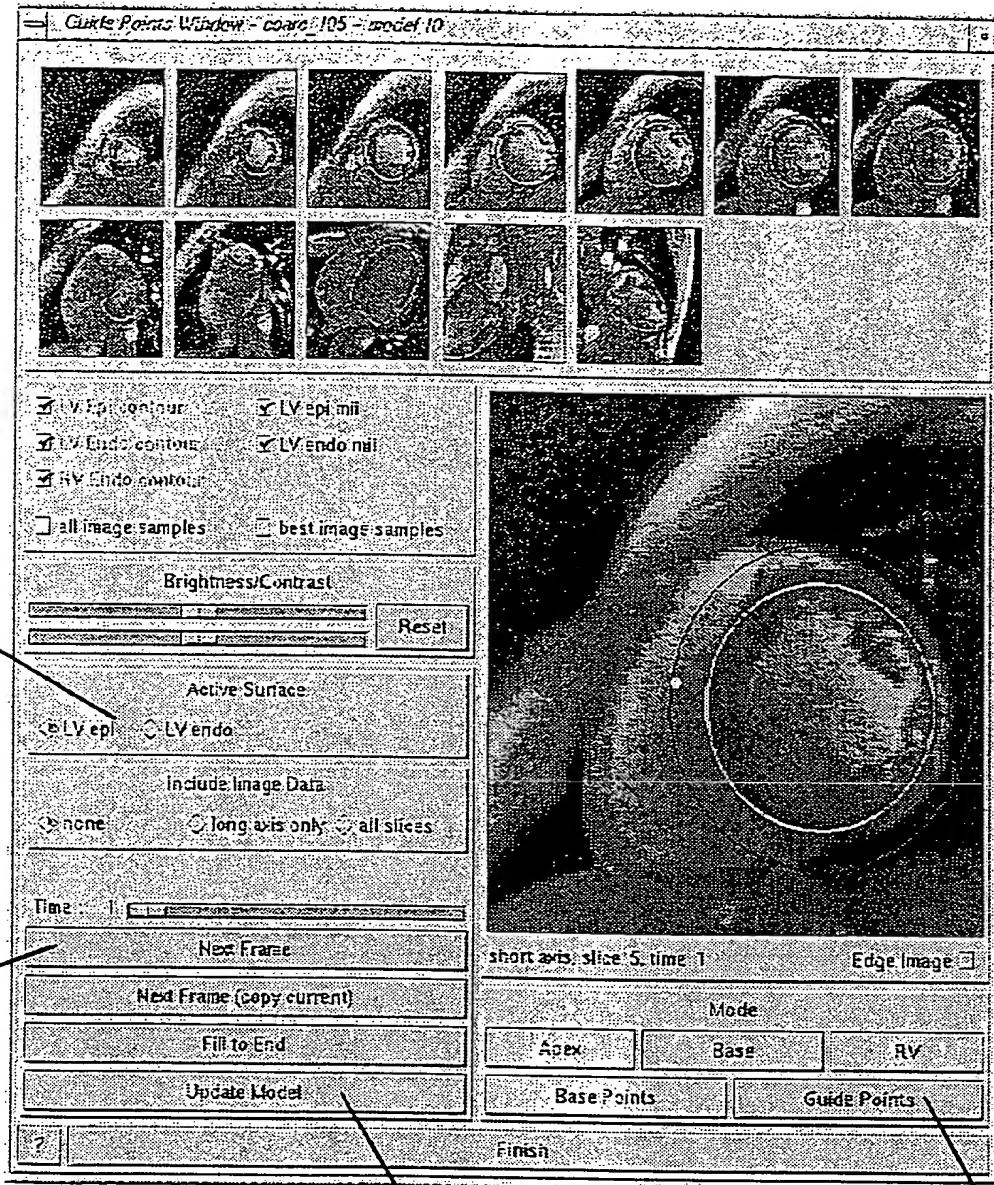
FIGURE 7
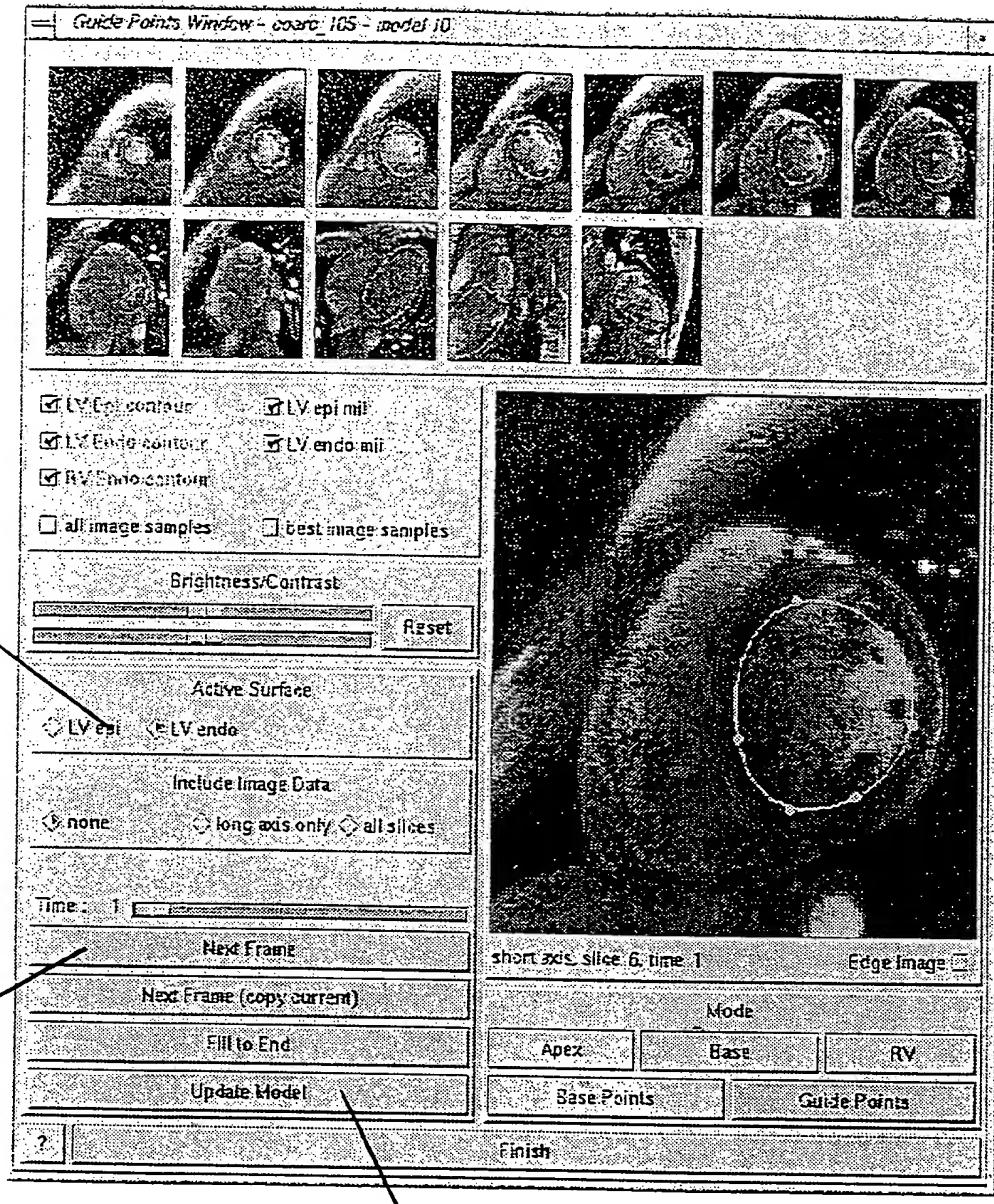
FIGURE 8
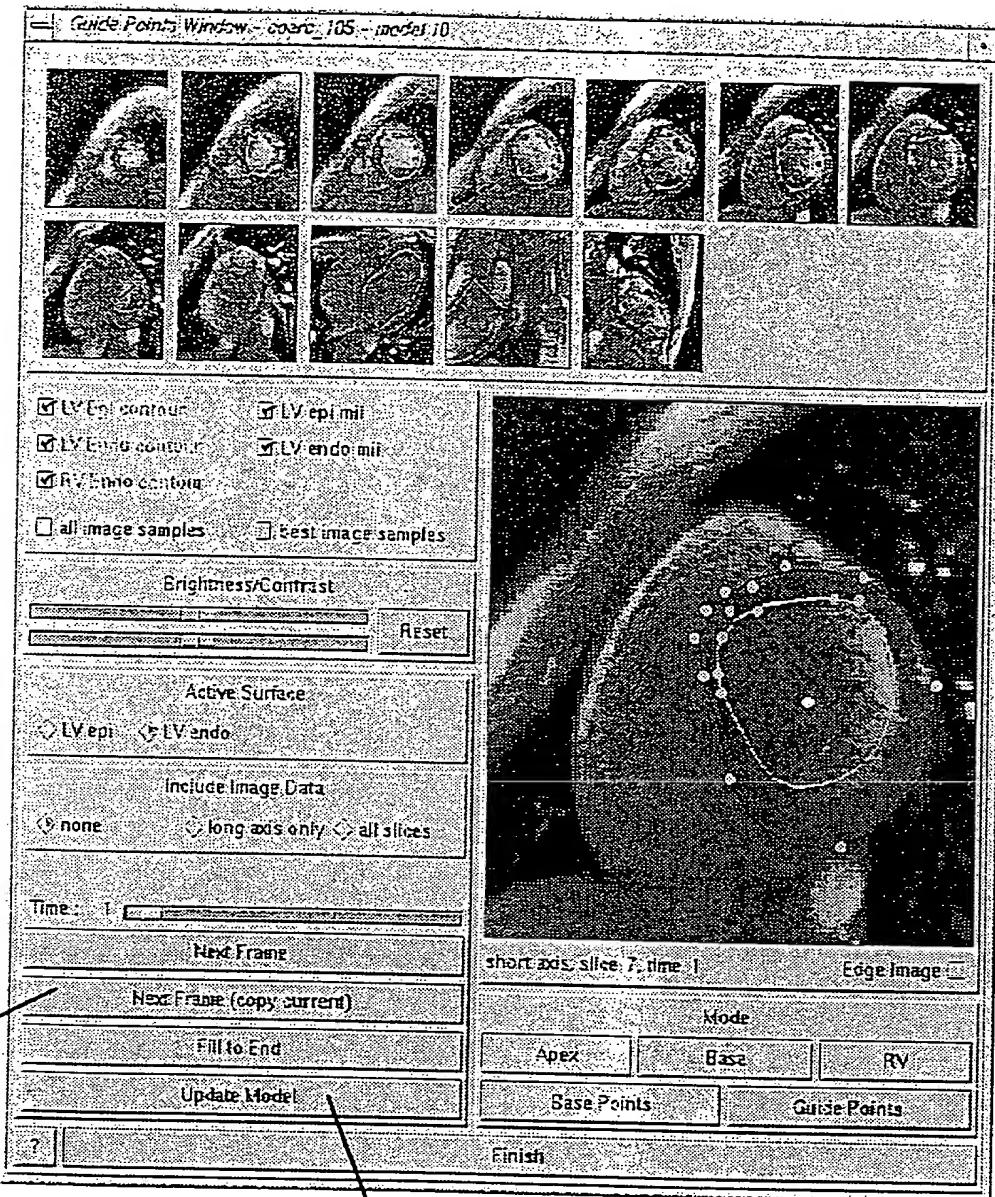
FIGURE 9
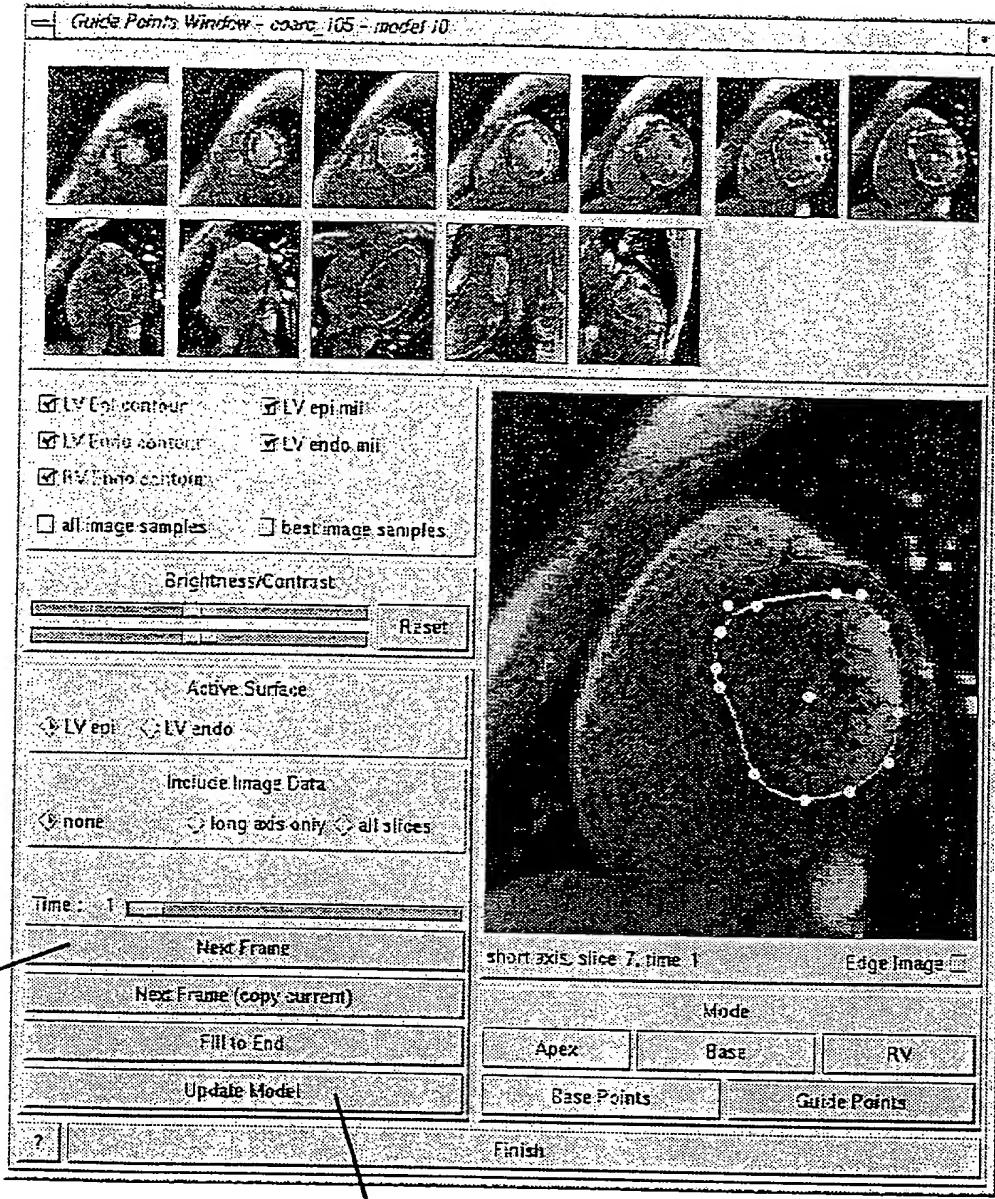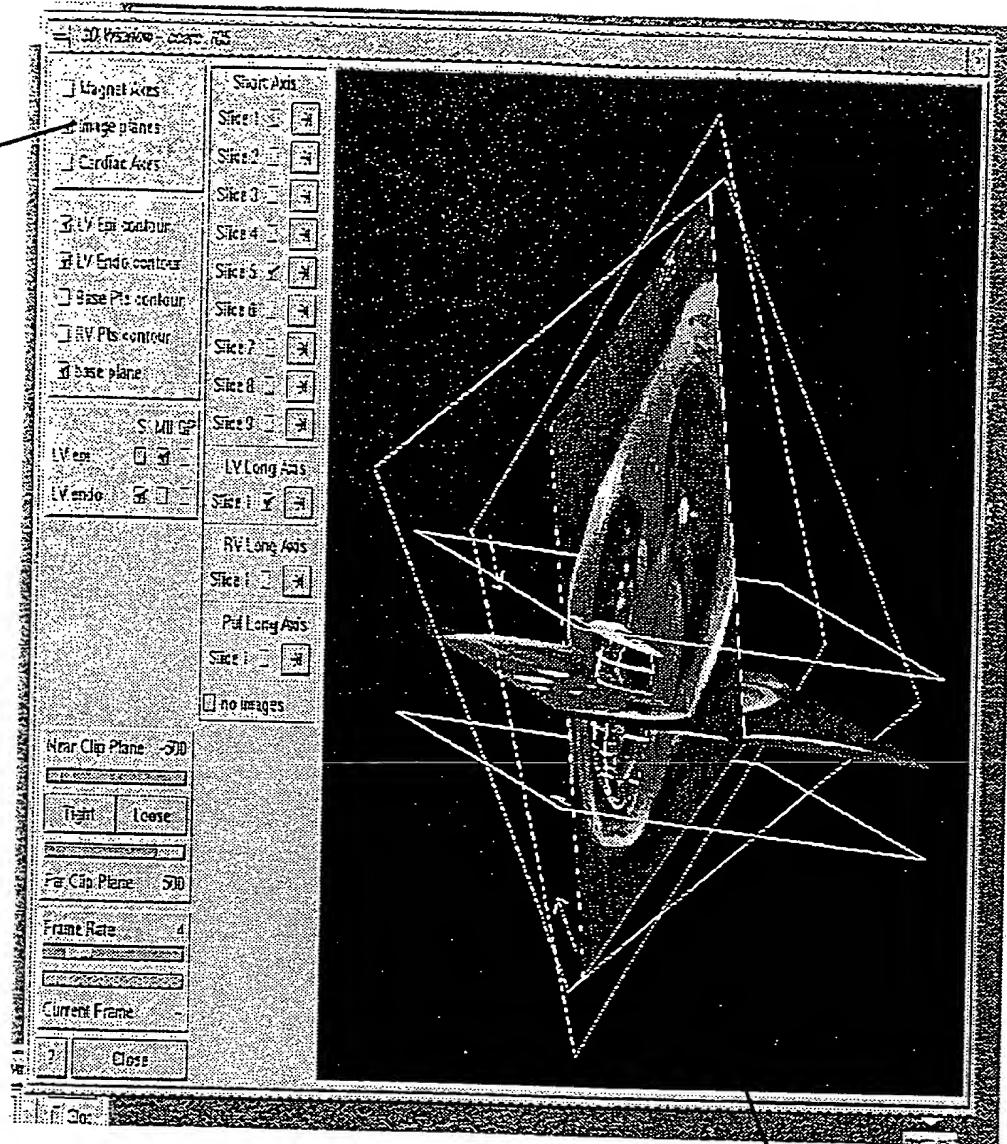
FIGURE 10

FIGURE 11

56

FIGURE 12

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